This document is the accepted manuscript version of the following article:
Prokhorov, I., & Mohn, J. (2022). CleanEx: a versatile automated methane preconcentration device for high-precision analysis of 13CH4, 12CH3D, and 13CH3D. Analytical Chemistry, 94(28), 9981-9986. https://doi.org/10.1021/acs.analchem.2c01949

CleanEx – A Versatile Automated Methane Preconcentration Device for High-Precision Analysis of $^{13}CH_4$, $^{12}CH_3D$, and $^{13}CH_3D$

Ivan Prokhorov* and Joachim Mohn

Laboratory for Air Pollution / Environmental Technology, Empa, 8600 Dübendorf, Switzerland

*Corresponding author: ivan.prokhorov@empa.ch

ABSTRACT: The relative abundance of methane isotopologues offers key insights into the global methane (CH_4) cycle. Advances in laser spectroscopy enable routine high-precision measurements even for rare deuterated methane isotopologues, $^{12}CH_3D$ and $^{13}CH_3D$, provided there are sufficiently high methane amount fractions and reproducible measurement conditions, which can be achieved by CH_4 adsorption-desorption techniques. We present a new cryogen-free automated preconcentration device – CleanEx – designed for quantitative extraction of CH_4 from large volumes of sample gas and for cleaning by stepwise temperature-controlled desorption to separate interferant gases. We show that CleanEx has the capability to preconcentrate methane by almost 2000-fold from ~18 L of air. The performance is demonstrated in a range of methane amount fractions between 2 ppm (μmol mol^{-1}), which corresponds to the present-day ambient air, up to 1000 ppm, representative for close to source or process conditions. Advantages over existing devices are a significantly larger primary adsorption trap and a secondary cryo-focusing step, which ensures separation of methane from major atmospheric compounds, i.e., O_2, Ar, and CO_2. We have demonstrated quantitative extraction of methane, with no significant isotopic fractionation and high repeatability of 0.2‰, 0.6‰, and 0.8‰ (n=42) for the studied isotopologue ratios, $^{13}CH_4/^{12}CH_4$, $^{12}CH_3D/^{12}CH_4$, and $^{13}CH_3D/^{12}CH_4$, during cryogenic adsorption-desorption on HayeSep D material. The developed device in combination with a suitable laser spectrometer offers a robust and autonomous method for precise continuous monitoring of $\delta^{13}C\text{-}CH_4$ and $\delta D\text{-}CH_4$ in ambient air and optionally $\Delta^{13}CH_3D$ in process-derived methane.

Methane (CH_4) is both an important fossil and regenerative energy source and a potent greenhouse gas and air pollutant. This poses multiple research questions with respect to origin and conditions of formation in energy exploration[1,2] but also in atmospheric budgeting.[3] Isotope ratios $^{13}C/^{12}C$ and D/H measured through singly substituted $^{13}CH_4$ and $^{12}CH_3D$ isotopologues are valuable tracers, which can help to distinguish the biogenic, abiotic, and thermogenic origins of methane (see, e.g., Menoud *et al.*[4] and references therein). Analyses of doubly substituted (clumped) isotopologues $^{13}CH_3D$ and $^{12}CH_2D_2$ provide independent constraints on formation temperature (for equilibrium processes), reaction mechanisms, mixing and destruction processes.[2,5]

The main analytical challenge of methane isotopologues analysis is the requirement for high analytical accuracy, generally in the sub-per-mille range, at low relative abundances. Measurements of $^{13}CH_4/^{12}CH_4$ ratios are routinely performed with commercial tunable mid-IR laser direct absorption and cavity-ring down spectrometers at atmospheric abundances[6,7] while $^{12}CH_3D/^{12}CH_4$ analysis in ambient air requires precedent preconcentration.[8,9] In case of doubly substituted isotopologue analysis, there are currently two competing analytical techniques, both applied on pure or high-concentration samples: high-resolution isotope ratio mass spectrometry (HR-IRMS)[10,11] and quantum cascade laser absorption spectroscopy (QCLAS)[12–16]. At the moment of writing, both methods are capable of achieving precision of better than 0.1‰ and 1‰ for $\Delta^{13}CH_3D$ and $\Delta^{12}CH_2D_2$, respectively.

Methane can be preconcentrated from ambient air or target process gases using cryogenic adsorption-distillation, making use of differences in boiling temperatures. Different high-volume, manual and liquid nitrogen[17] or low-volume, automated, and cryogen-free[18,19] devices have been realized and integrated into mass spectrometry workflows.[20] Laser spectroscopic analyses of deuterated $^{12}CH_3D$ and $^{13}CH_3D$ isotopologues pose distinct challenges with respect to preconcentration, in particular the requirement for higher sample volumes, and the need for automated, cryogen-free operations to enable continuous lab or field operations. Published preconcentration devices,[8,9] however, are optimized for only 0.4 – 0.6 μmol CH_4 from 5 – 7.5 L of air and do not achieve preconcentration factors required for clumped isotope analysis. Besides, one-trap systems have shown difficulties with quantitative separation from oxygen.[8]

In this study, we extend the performance of automated, cryogen-free preconcentration systems for laser spectroscopic analyses of rare CH_4 isotopologues. The objective of the further developments is twofold: (1) Enhance the preconcentration factor for CH_4 extraction from ambient air implementing a second cryo-focusing trap to improve separation of bulk gases and enable high-precision and accurate optical analysis of isotopologue ratios in ~1 μmol CH_4 samples; (2) Enlarge the capacity of the preconcentration device to process ≥50 μmol CH_4 extracted from process-specific samples at elevated CH_4 mole fraction to enable optical $\Delta^{13}CH_3D$ analysis.

EXPERIMENTAL SECTION

The **Clean**ing and **Ex**tracting unit presented in this technical note **CleanEx** is a further development in a family of fully automated cryogen-free **Tr**ace gas **Ex**tractors (TREX) designed for nitrous oxide[21] and methane[8] extraction from ambient air and subsequent isotope analysis with a laser spectrometer. TREXs shared a common design platform equipped with a detachable trap and gas flow scheme inherited from Medusa,[22] and are fully automated by a customized LabView (National Instruments, USA) code developed for autonomous operation. The main upgrade of the new unit with respect to the previous generation is threefold: (1) a 50% enlarged amount of adsorbent in the primary trap, (2) a lower operating temperature of the primary trap (T1) at –171°C, and (3) a secondary cryo-focusing trap (T2). With these modifications, we address a

major limitation of the previous TREX unit,[8] namely, an elevated oxygen content in the processed sample. The latter leads to an offset in $\delta^{13}C\text{-}CH_4$ measurements due to the induced matrix effect, which has to be characterized and post-corrected.[23] Complete removal of oxygen thus significantly simplifies the instrument's calibration and correction scheme.

Method Overview. The basic principle of methane extraction and purification is based on the separation of air constituents by their boiling point temperatures. Stepwise temperature control of the absorbent combined with flushing of the absorbent-filled traps by a carrier gas allows separation of methane (boiling point, −161.5 °C; mole fraction in dry ambient air, 1889±2 ppb)[24] from major dry air compounds with a lower boiling point, i.e., N_2, O_2, Ar, CO, and trace gases with a higher boiling point, i.e., Kr, N_2O, CO_2.

It is critically important for isotope analysis to minimize changes in isotopologue ratios, called fractionation effects, which is generally ensured by quantitatively complete recovery of the methane fraction. Therefore, significant effort has been invested toward optimization of the cooling and heating cycles of the traps, the choice of carrier gas flows, and the optimal timing of sample refocusing from T1 to T2.

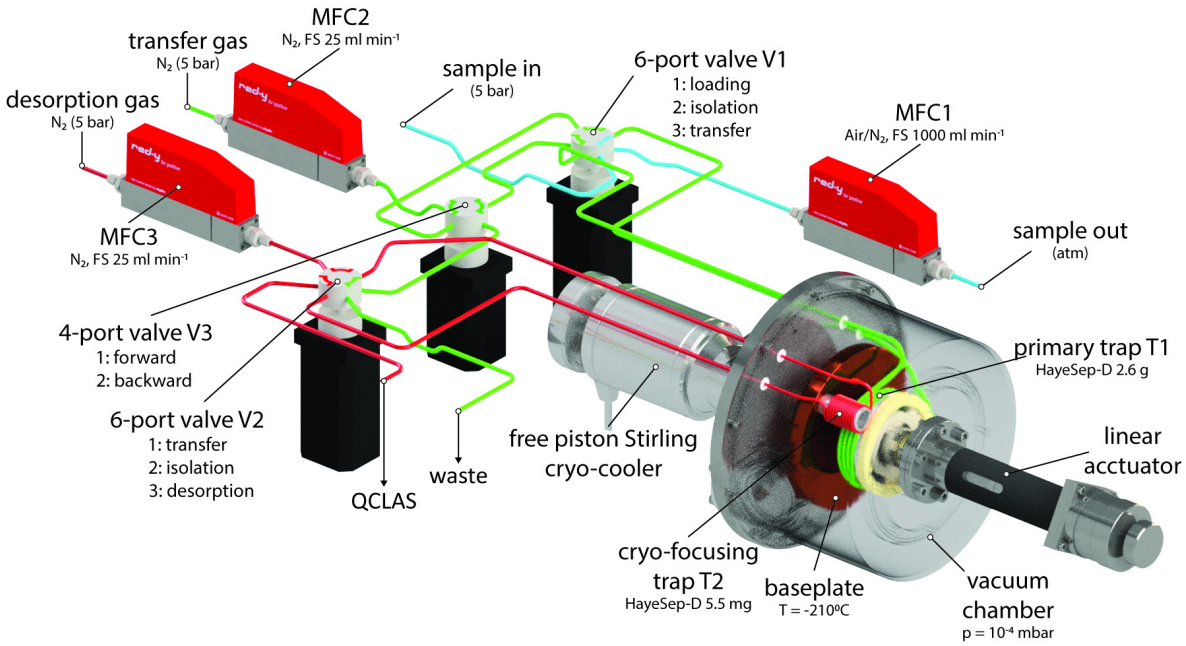


Figure 1. Simplified depiction of the CleanEx flow layout for methane preconcentration and introduction into a QCLAS device. Multiport valve V1 controls the sample flow through the primary trap (T1) or isolates the trap. V2 changes the flow direction (forward vs backward) through T1. V3 controls the sample transfer onto the cryo-focusing trap (T2) by connecting the traps in series, or isolates T2. Mass flow controllers MFC1-3 regulate the flows of the sample, transfer, and desorption gas, respectively. The stainless-steel vacuum chamber, shown transparent for clarity, is evacuated with a turbo-molecular pump to avoid condensation on the cooled parts.

Preconcentration Unit Design and Operation. The primary trap (T1, light green colored coil in Figure 1) is made of an electropolished stainless-steel tube (3 mm i.d., 4 mm o.d., total length 1 m) twisted in a coil (3.5 turns) around an aluminum standoff (80 mm o.d.). The middle part (85 cm) of the coil is filled with 2.6 g of the HayeSep D porous polymer adsorbent (Sigma-Aldrich, Merck KGaA, Germany). Glass wool insertions (20 mm on both sides) and mesh wire insertions (50 mm at the entrance and 25 mm at the exit) mechanically retain the adsorbent, cool the gas, and partially adsorb gases with higher boiling points, e.g., CO_2 and N_2O. The standoff is mounted on a linear actuator contacted with a wave spring, which ensures even and adjustable force distribution between standoff and baseplate. Rapid cooling of the trap is achieved by pressing the standoff against the massive copper baseplate (diameter 14 cm, thickness 1 cm). The temperature of the baseplate is maintained at –215°C by a free-piston Stirling cryocooler (capacity 10 W, CryoTel GT, Sunpower, Inc., USA), monitored by a Type-K thermocouple. The heat sink of the cryocooler is stabilized at 18°C by a liquid recirculating chiller (ThermoRack 801, SolidState Cooling Systems, USA). Good thermal contact is ensured by polishing the baseplate (roughness 0.2 µm) and standoff surfaces and by applying a thin layer of thermo-conductive paste (340 HSC, Dow Croning, USA). For desorption and conditioning, T1 is detached from the baseplate and heated by a polyamide heating pad (Minico Products, Inc., USA). The trap temperature is monitored with a Pt-102 sensor inserted into the standoff body and precisely controlled using a PID controller (diraTron, Jumo AG, Switzerland). PID parameters were optimized to stabilize the temperature of the trap around −171°C and to provide rapid heating to target temperatures, yet to prevent overshoot.

A cryo-focusing trap (T2, red colored coil in Figure 1) made of a 1/16 in. o.d stainless steel tube and containing 5.5 mg of HayeSep D is coiled (seven turns) onto a 17 mm thin-walled standoff. The temperature of T2 is monitored by a Type-E thermocouple and resistively heated applying high current (7.5 A), using custom-made electronics, regulated by a PID controller (diraTron, Jumo AG, Switzerland).

T1 and T2 are integrated in the instrument's flow layout as shown in Figure 1. Six-port valves V1 and V2 (Valco Instruments Inc., Switzerland) are installed to regulate gas flows toward T1 and T2, respectively, and isolate the traps during cooling phases. The four-port valve V3 (Valco Instruments Inc., Switzerland) regulates the flow direction through T1. Three mass flow controllers MFC1-3 (Red-y Smart Series, Vögtlin Instruments, Switzerland, calibrated at 20°C) are deployed for reproducible and precise flow control of the sample gas (MFC1, full scale 1000 mL min^{-1}), and transfer as well as desorption gas N_2 (MFC2-3, full scales 25 mL min^{-1}).

The operation sequence and parameter settings were optimized to ensure quantitative adsorption on the primary trap, complete desorption of methane from T1 and refocusing on T2, and efficient

elution from T2. An exemplary preconcentration cycle is presented in Figure S1 together with a description of major operation phases.

RESULTS AND DISCUSSION

Versatile operation of the preconcentration device CleanEx relies on several factors: sufficient adsorption capacity to process required amounts of methane, effective separation of methane from other sample gas constituents to avoid spectral interferences and matrix variation induced errors, desirable enhancement in CH_4 concentration between input and output samples to match the operation requirements of the laser spectrometer, and finally, reproducible operation with quantitative isotopologue extraction to avoid or minimize isotopic fractionation. These factors were extensively studied as presented in the following sections.

Adsorption Capacity. One of the design criteria for the presented setup compared to earlier versions and solutions realized for IRMS analysis was to enhance and test its capability to process large amounts of CH_4 suitable for analysis of clumped isotopes by QCLAS. The total amount of CH_4 that can be processed by CleanEx is limited by the maximum sample volume processed before CH_4 exits the primary trap, named adsorption capacity. If further cleaning of the CH_4 sample is required, readsorption on T2 has to be tested as well. Preliminary experiments indicated that the adsorption capacity for CH_4 is a function of trap temperature, sample flow rate, and CH_4 concentration in the sample gas.

In a specific set of experiments, the adsorption capacity of the primary trap was tested at three trap temperatures below the boiling point of methane (–166, –171, –176°C) and three sample flow rates (500, 700, 900 mL min^{-1}) for CH_4 concentrations typical for ambient air (2.0 ppm of CH_4 in whole air) and process-level (1000 ppm of CH_4 in synthetic air) applications. The tested lowest trap temperature (–176°C) and highest flow rate (900 mL min^{-1}) represent threshold values for T1 in the current CleanEx configuration.

Results presented in Figure 2A indicate a strong increase of the adsorption capacity with lower trap temperatures and a weaker, inconsistent dependence on the flow rate at ambient CH_4 mole fractions. One should keep in mind, however, that the indicated trap temperature represents the actual temperature at the sensor location but not the temperature inside the tubing, i.e. where gas molecules are actually adsorbed. This might explain the fact, that for a given trap temperature (e.g., –176°C) at high flow rates the adsorbed volumes of oxygen and nitrogen are lower (160 mL at 900 mL min^{-1} and 214 mL at 500 mL min^{-1}, respectively). At any temperature of T1 CleanEx is capable of extracting more than sufficient amounts (1.5 µmol) of CH_4 from air required for precise δD-CH_4 analysis by a dual laser QCLAS (Aerodyne Research, Inc.) requiring 0.5 µmol CH_4.[8,9]

The adsorption capacity of the primary trap shows little dependence on the CH_4 amount fraction in the sample. In a wide range of mole fractions between 2 and 1000 ppm, the adsorption capacity was above 17 L, when the trap temperature was set to –176°C and the flow of the sample was 900 mL min^{-1}. At a very high methane mole fraction of 2% in a synthetic air matrix, the adsorption capacity was still 11 L under the same experimental conditions. Consequently, at CH_4 amount fractions in the sample gas of 1000 ppm or even at percent levels, typical for process applications, sufficient CH_4 for precise analysis of $\Delta^{13}CH_3D$ (50 µmol) and even $\Delta^{12}CH_2D_2$ (500 µmol) can be preconcentrated.

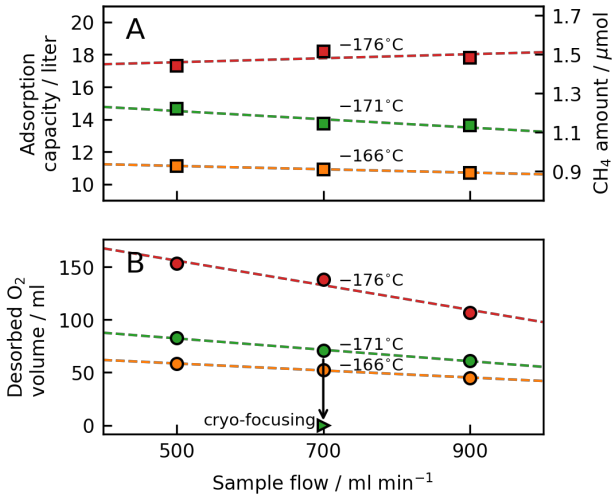


Figure 2. (A) Adsorption capacity of the primary trap for sample gas with ambient concentrations and corresponding methane amount. (B) total volume of oxygen desorbed from T1 (circles) for different trap temperatures as a function of sample flow rate and for one exemplary flow rate after cryo-focusing on T2 (triangle). Dashed lines are linear interpolations.

Depending on the specific application, a second cryo-focusing step on T2 of CleanEx might be required, for example, to quantitatively separate O_2 from an ambient air matrix. T2 was designed as a permanently attached (nonmoveable) trap. For pure CH_4 samples, T2 was capable to adsorb 15±2 mL at 5 mL min^{-1} flow rate. For cryo-focusing of methane extracted from ambient air or process gases and desorbed from T1, CH_4 is accompanied by coadsorbed gases (mainly, N_2, O_2), which limits the adsorption capacity of T2. Quantitative CH_4 transfer and readsorption on T2 were demonstrated for ambient air even at high sample volumes (18 L STP). Efficient transfer is only possible when the exit of T2 was blocked for the initial phase of transfer. This prevents intrusion of ambient air which would otherwise contaminate and heat the trap due to adsorption of atmospheric gas compounds.For process-level CH_4 input concentrations, systematic tests with CH_4 amounts of 0.5 – 10 mL (STP) and trap temperatures of $T_{T1} = 0°C$ and $T_{T2} = -186°C$ display that breakthrough of T2 happens after a 5 min transfer with a 5 mL min^{-1} N_2 flow for any sample larger than 1.5 ml CH_4. This indicate that with the current T2 design sufficient CH_4 (67 µmol, 1.5 mL STP) for precise $\Delta^{13}CH_3D$ analysis by QCLAS can be quantitatively readsorbed. For precise analysis of $\Delta^{12}CH_2D_2$, the current capacity of T2 seems to be insufficient and would have to be replaced by a larger cryo-focusing trap. In the dual trap configuration presented in this study, we achieve 2000 - fold enhancement for ambient air samples of 15 L. The calculation of enhancement factors is presented in eq. S1 Supporting Information S3.

Separation Efficiency. A major limitation of existing preconcentration devices is the insufficient separation of bulk air constituents (e.g., O_2, Ar, Kr) having boiling point temperatures close to CH_4. Variations in the amount fractions of bulk air constituents affect the pressure broadening of the analyzed CH_4 lines, limiting the accuracy of optical analyzers.[8] This effect is highly relevant for He and Ar, since their broadening coefficients are very different from nitrogen,[25] and to a lesser extent for krypton, whose broadening coefficient is very similar to that of nitrogen.[26] Therefore, one stimulus for the dual trap design of the CleanEx device was the urge for quantitative separation of O_2. Since we use high-purity nitrogen as a transfer and desorption gas, coadsorption of N_2 does not affect the gas matrix composition.

Oxygen coadsorption on T1 was systematically tested for different trap temperatures (–166, –171 and –176°C) and sample flow

rates (500, 700, 900 mL min^{-1}) along with the determination of CH_4 adsorption capacity described before. For this, the O_2 amount fraction at the outlet of T1 was monitored during desorption with a paramagnetic analyzer (570A, Serovemex, UK) and the desorbed O_2 volume calculated as an integrated flow through the mass flow controller installed downstream of the primary trap. Results presented in Figure 2B indicate that higher amounts of O_2 are coadsorbed at lower T1 temperatures and lower adsorption flows, with the latter being rationalized by lower effective temperatures of the HayeSep D adsorbent. Partial removal of coadsorbed gases was accomplished implementing a stepwise heating profile of T1 (Figure S1C) before transfer of CH_4 and remaining coadsorbed gases on T2.

To monitor the selectivity of the complete two trap process for CH_4 separation, the bulk gas composition (O_2, Ar, Kr) of the gas matrix after desorption from T2 was analyzed by mass spectrometry (QMS, Vision 1000-C, MKS Instruments, Inc., USA). Concentration profiles of the desorbed gases (Figure S1E) demonstrate that no significant coadsorption of O_2 (< 0.5%) and Ar (< 0.02%) occurs. Krypton, however, which has a boiling point of only 8°C higher than methane and a mixing ratio of ~1 ppm in the atmosphere, is coeluted with CH_4, and cryogenic separation remains very challenging.

Isotopic Fractionation and Repeatability. An important characteristic of a preconcentration device for subsequent isotope analysis is the absence or at least constancy of changes in the isotopic composition of the target substance between input and output samples.

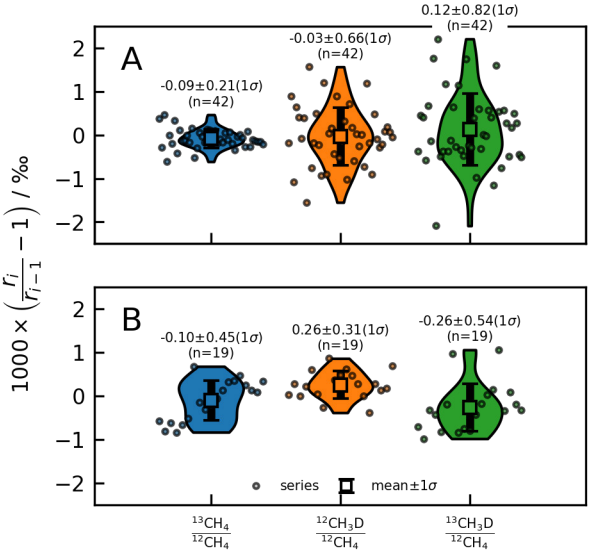


Figure 3. (A) Reproducibility of isotopologue ratio measurements for subsequent dual trap preconcentration cycles. (B) Magnitude of isotopic fractionation associated with methane extraction.

In the first step, we quantified the reproducibility of isotopologue ratios for 42 subsequent preconcentration cycles for a gravimetrically prepared 1000.4 (±1% rel.) ppm of CH_4 in a N_2 mixture. In this experimental series (Figure 3A), each desorbed sample acted as a reference point for the following sample. Standard deviations of 0.2‰, 0.7‰ and 0.8‰ were determined for $^{13}CH_4/^{12}CH_4$, $^{12}CH_3D/^{12}CH_4$, and $^{13}CH_3D/^{12}CH_4$, respectively, resulting in the respective standard errors (1 S.E., n = 42) of 0.03‰, 0.11‰, and 0.12‰. The demonstrated high reproducibility ensures a close link between reference and sample measurements, when using an identical treatment approach, i.e., preconcentration of both gases. However, this experiment is insensitive to the presence of isotope fractionation effects, which we quantified in another set of extractions described below. The average recovery yield was determined from the CH_4 amount adsorbed on and desorbed from T1 in a separate experiment, which confirmed the quantitative recovery (99±2%, n = 42).

In the second experiment, we estimated the magnitude of isotope fractionation in a series (n = 19) of extraction cycles, when the in-house working reference ($\delta^{13}C_{VPDB}$ = –44.21±0.15‰, δD_{VSMOW} = –189.0±1‰, 99.9995% CH_4) was dynamically diluted with N_2 in a 1:1000 ratio (1000 ppm of CH_4) before being processed by CleanEx. Figure 3B shows isotopologue ratios analyzed by QCLAS in the processed sample referenced to the undiluted / unprocessed CH_4 in N_2 gas. Details on QCLAS performance are given in Supporting Information S2. The effect of differences in CH_4 amount fractions on isotopologue ratios was corrected (Table S1). The mean observed deviations of –0.1‰, 0.3‰, and –0.3‰ for $\delta^{13}C$-CH_4, δD-CH_4, and $\delta^{13}CH_3D$, respectively, are within one standard deviation of the measurements, which indicates that fractionation effects are not significant. In comparison with the previously reported preconcentration devices capable of direct deuterated methane measurements, we have achieved almost twofold improvement in uncertainty for $^{12}CH_3D/^{12}CH_4$ and for the first time demonstrated the capability for doubly substituted clumped $^{13}CH_3D$ analysis.

CONCLUSION

We have developed and characterized a fully automated cryogen-free preconcentration unit to enhance the mole fraction of methane by a factor of 2000 from the ambient level and enable precise and accurate laser spectroscopic analysis of $^{12}CH_3D$ in ambient methane. The maximum amount of methane that can be processed in a two-trap configuration from process level concentrations (1000 ppm of CH_4) is as high as 0.67 mmol (1.5 mL STP). This amount is sufficient to enable direct high-precision analysis of doubly substituted (clumped) isotopologue $^{13}CH_3D$. Quantitative and reproducible methane recovery without significant fractionation effects for isotopologue ratios $^{13}CH_4/^{12}CH_4$, $^{12}CH_3D/^{12}CH_4$, and $^{13}CH_3D/^{12}CH_4$ has been demonstrated in this study. The developed device can be adapted for analysis of other rare isotopic species.

ACKNOWLEDGMENT

This work was financially supported by the Swiss National Science Foundation (SNSF) under R'Equip project QCL4CLUMPS (no. 206021_183294) and CLUMPME (no. 200021_200977), and the project 19ENV05 STELLAR, which has received funding from the EMPIR programme co-financed by the Participating States and from the European Union's Horizon 2020 research and innovation programme. The authors acknowledge the contribution of Urs Hintermüller, Arno Aeschbacher, Andrin Moosmann, Erwin Pieper, and the team of the Empa mechanical workshop to the setup manufacturing and assembly. We thank Philipp Scheidegger for electronics development, André Kupferschmid for LabView code optimization, and Christoph Zellweger from WMO-GAW WCC for providing a Picarro G-2401 GHG analyzer.

SUPPORTING INFORMATION

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.analchem.2c01949

Exemplary preconcentration unit operation cycle with detailed description of each phase; statement on the performance of QCLAS; mathematical calculation of enhancement factor; traps breakthrough measurement protocol. Data underlying the results presented in this paper is available online.[27]

AUTHOR CONTRIBUTIONS

Ivan Prokhorov optimized and tested the preconcentration device, designed and conducted laboratory experiments, and analyzed the data. Joachim Mohn conceptualized and supervised the project, and

discussed the results. The manuscript was written with contributions of both authors. Both authors have given approval to the final version of the manuscript. The authors declare no competing financial interest.

REFERENCES

(1) Stolper, D. A.; Martini, A. M.; Clog, M.; Douglas, P. M.; Shusta, S. S.; Valentine, D. L.; Sessions, A. L.; Eiler, J. M. Distinguishing and Understanding Thermogenic and Biogenic Sources of Methane Using Multiply Substituted Isotopologues. *Geochimica et Cosmochimica Acta* **2015**, *161*, 219–247. https://doi.org/10.1016/j.gca.2015.04.015.

(2) Douglas, P. M. J.; Stolper, D. A.; Eiler, J. M.; Sessions, A. L.; Lawson, M.; Shuai, Y.; Bishop, A.; Podlaha, O. G.; Ferreira, A. A.; Santos Neto, E. V.; Niemann, M.; Steen, A. S.; Huang, L.; Chimiak, L.; Valentine, D. L.; Fiebig, J.; Luhmann, A. J.; Seyfried, W. E.; Etiope, G.; Schoell, M.; Inskeep, W. P.; Moran, J. J.; Kitchen, N. Methane Clumped Isotopes: Progress and Potential for a New Isotopic Tracer. *Organic Geochemistry* **2017**, *113*, 262–282. https://doi.org/10.1016/j.orggeochem.2017.07.016.

(3) Nisbet, E. G.; Dlugokencky, E. J.; Fisher, R. E.; France, J. L.; Lowry, D.; Manning, M. R.; Michel, S. E.; Warwick, N. J. Atmospheric Methane and Nitrous Oxide: Challenges Alongthe Path to Net Zero. *Phil. Trans. R. Soc. A.* **2021**, *379* (2210), 20200457. https://doi.org/10.1098/rsta.2020.0457.

(4) Menoud, M.; van der Veen, C.; Lowry, D.; Fernandez, J. M.; Bakkaloglu, S.; France, J. L.; Fisher, R. E.; Maazallahi, H.; Stanisavljević, M.; Nęcki, J.; Vinkovic, K.; Łakomiec, P.; Rinne, J.; Korbeń, P.; Schmidt, M.; Defratyka, S.; Yver-Kwok, C.; Andersen, T.; Chen, H.; Röckmann, T. *Global Inventory of the Stable Isotopic Composition of Methane Surface Emissions, Augmented by New Measurements in Europe*; preprint; Atmosphere – Atmospheric Chemistry and Physics, 2022. https://doi.org/10.5194/essd-2022-30.

(5) Chung, E.; Arnold, T. Potential of Clumped Isotopes in Constraining the Global Atmospheric Methane Budget. *Global Biogeochem Cycles* **2021**, *35* (10). https://doi.org/10.1029/2020GB006883.

(6) Santoni, G. W.; Lee, B. H.; Goodrich, J. P.; Varner, R. K.; Crill, P. M.; McManus, J. B.; Nelson, D. D.; Zahniser, M. S.; Wofsy, S. C. Mass Fluxes and Isofluxes of Methane (CH_4) at a New Hampshire Fen Measured by a Continuous Wave Quantum Cascade Laser Spectrometer. *Journal of Geophysical Research: Atmospheres* **2012**, *117* (D10). https://doi.org/10.1029/2011JD016960.

(7) Hoheisel, A.; Yeman, C.; Dinger, F.; Eckhardt, H.; Schmidt, M. An Improved Method for Mobile Characterisation of $\delta^{13}CH_4$ Source Signatures and Its Application in Germany. *Atmos. Meas. Tech.* **2019**, *12* (2), 1123–1139. https://doi.org/10.5194/amt-12-1123-2019.

(8) Eyer, S.; Tuzson, B.; Popa, M. E.; van der Veen, C.; Röckmann, T.; Rothe, M.; Brand, W. A.; Fisher, R.; Lowry, D.; Nisbet, E. G.; Brennwald, M. S.; Harris, E.; Zellweger, C.; Emmenegger, L.; Fischer, H.; Mohn, J. Real-Time Analysis of δ^{13}C- and δD-CH_4 in Ambient Air with Laser Spectroscopy: Method Development and First Intercomparison Results. *Atmos. Meas. Tech.* **2016**, *9* (1), 263–280. https://doi.org/10.5194/amt-9-263-2016.

(9) Rennick, C.; Arnold, T.; Safi, E.; Drinkwater, A.; Dylag, C.; Webber, E. M.; Hill-Pearce, R.; Worton, D. R.; Bausi, F.; Lowry, D. Boreas: A Sample Preparation-Coupled Laser Spectrometer System for Simultaneous High-Precision In Situ Analysis of $\delta^{13}C$ and $\delta^{2}H$ from Ambient Air Methane. *Anal. Chem.* **2021**, *93* (29), 10141–10151. https://doi.org/10.1021/acs.analchem.1c01103.

(10) Eldridge, D. L.; Korol, R.; Lloyd, M. K.; Turner, A. C.; Webb, M. A.; Miller, T. F.; Stolper, D. A. Comparison of Experimental vs Theoretical Abundances of $^{13}CH_3D$ and $^{12}CH_2D_2$ for Isotopically Equilibrated Systems from 1 to 500°C. *ACS Earth Space Chem.* **2019**, *3* (12), 2747–2764. https://doi.org/10.1021/acsearthspacechem.9b00244.

(11) Young, E. D.; Rumble, D.; Freedman, P.; Mills, M. A Large-Radius High-Mass-Resolution Multiple-Collector Isotope Ratio Mass Spectrometer for Analysis of Rare Isotopologues of O-2, N-2, CH4 and Other Gases. *International Journal of Mass Spectrometry* **2016**, *401*, 1–10. https://doi.org/10.1016/j.ijms.2016.01.006.

(12) Ono, S.; Wang, D. T.; Gruen, D. S.; Sherwood Lollar, B.; Zahniser, M. S.; McManus, B. J.; Nelson, D. D. Measurement of a Doubly Substituted Methane Isotopologue, $^{13}CH_3D$, by Tunable Infrared Laser Direct Absorption Spectroscopy. *Anal. Chem.* **2014**, *86* (13), 6487–6494. https://doi.org/10.1021/ac5010579.

(13) Gonzalez, Y.; Nelson, D. D.; Shorter, J. H.; McManus, J. B.; Dyroff, C.; Formolo, M.; Wang, D. T.; Western, C. M.; Ono, S. Precise Measurements of $^{12}CH_2D_2$ by Tunable Infrared Laser Direct Absorption Spectroscopy. *Anal. Chem.* **2019**, *91* (23), 14967–14974. https://doi.org/10.1021/acs.analchem.9b03412.

(14) Prokhorov, I.; Kluge, T.; Janssen, C. Laser Absorption Spectroscopy of Rare and Doubly Substituted Carbon Dioxide Isotopologues. *Anal. Chem.* **2019**, *91* (24), 15491–15499. https://doi.org/10.1021/acs.analchem.9b03316.

(15) Wang, Z.; Nelson, D. D.; Dettman, D. L.; McManus, J. B.; Quade, J.; Huntington, K. W.; Schauer, A. J.; Sakai, S. Rapid and Precise Analysis of Carbon Dioxide Clumped Isotopic Composition by Tunable Infrared Laser Differential Spectroscopy. *Anal. Chem.* **2020**, *92* (2), 2034–2042. https://doi.org/10.1021/acs.analchem.9b04466.

(16) Nataraj, A.; Gianella, M.; Prokhorov, I.; Tuzson, B.; Bertrand, M.; Mohn, J.; Faist, J.; Emmenegger, L. Quantum Cascade Laser Absorption Spectrometer with a Low Temperature Multipass Cell for Precision Clumped CO_2 Measurement. *Opt. Express* **2022**, *30* (3), 4631. https://doi.org/10.1364/OE.447172.

(17) Espic, C.; Liechti, M.; Battaglia, M.; Paul, D.; Röckmann, T.; Szidat, S. Compound-Specific Radiocarbon Analysis of Atmospheric Methane: A New Preconcentration and Purification Setup. *Radiocarbon* **2019**, *61* (5), 1461–1476. https://doi.org/10.1017/RDC.2019.76.

(18) Brand, W. A.; Rothe, M.; Sperlich, P.; Strube, M.; Wendeberg, M. Automated Simultaneous Measurement of the $\delta^{13}C$ and $\delta^{2}H$ Values of Methane and the $\delta^{13}C$ and $\delta^{18}O$ Values of Carbon Dioxide in Flask Air Samples Using a New Multi Cryo-Trap/Gas Chromatography/Isotope Ratio Mass Spectrometry System: $\delta^{13}C$, $\delta^{2}H$ and $\delta^{18}O$ Values of CH_4 and CO_2. *Rapid Commun. Mass Spectrom.* **2016**, *30* (13), 1523–1539. https://doi.org/10.1002/rcm.7587.

(19) Umezawa, T.; Andrews, S. J.; Saito, T. A Cryogen-Free Automated Measurement System of Stable Carbon Isotope Ratio of Atmospheric Methane. *Journal of the Meteorological Society of Japan* **2020**, *98* (1), 115–127. https://doi.org/10.2151/jmsj.2020-007.

(20) Brass, M.; Röckmann, T. Continuous-Flow Isotope Ratio Mass Spectrometry Method for Carbon and Hydrogen Isotope Measurements on Atmospheric Methane. *Atmospheric Measurement Techniques* **2010**, *3* (6), 1707–1721. https://doi.org/10.5194/amt-3-1707-2010.

(21) Ibraim, E.; Harris, E.; Eyer, S.; Tuzson, B.; Emmenegger, L.; Six, J.; Mohn, J. Development of a Field-Deployable Method for Simultaneous, Real-Time Measurements of the Four Most Abundant N_2O Isotopocules. *Isotopes in Environmental and Health Studies* **2018**, *54* (1), 1–15. https://doi.org/10.1080/10256016.2017.1345902.

(22) Miller, B. R.; Weiss, R. F.; Salameh, P. K.; Tanhua, T.; Greally, B. R.; Mühle, J.; Simmonds, P. G. Medusa: A Sample Preconcentration and GC/MS Detector System for in Situ Measurements of Atmospheric Trace Halocarbons, Hydrocarbons, and Sulfur Compounds. *Anal. Chem.* **2008**, *80* (5), 1536–1545. https://doi.org/10.1021/ac702084k.

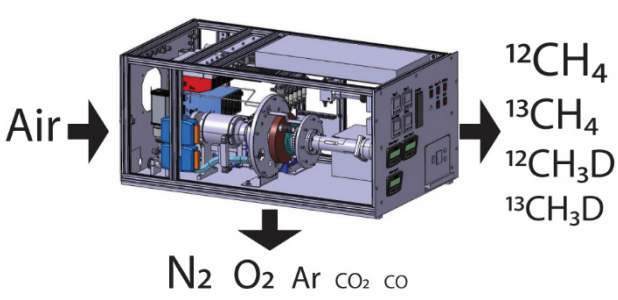
(23) Harris, S. J.; Liisberg, J.; Xia, L.; Wei, J.; Zeyer, K.; Yu, L.; Barthel, M.; Wolf, B.; Kelly, B. F. J.; Cendón, D. I.; Blunier, T.; Six, J.; Mohn, J. N_2O Isotopocule Measurements Using Laser Spectroscopy: Analyzer Characterization and Intercomparison. *Atmos. Meas. Tech.* **2020**, *13* (5), 2797–2831. https://doi.org/10.5194/amt-13-2797-2020.

(24) *The State of Greenhouse Gases in the Atmosphere Based on Global Observations through 2020*; Greenhouse Gas Bulletin; 17; World Meteorological Organization (WMO), 2021; p 10.

(25) Pine, A. S. Self-, N_2, O_2, H_2, Ar, and He Broadening in the ν_3 Band *Q* Branch of CH_4. *The Journal of Chemical Physics* **1992**, *97* (2), 773–785. https://doi.org/10.1063/1.463943.

(26) Zéninari, V.; Parvitte, B.; Courtois, D.; Kapitanov, V. A.; Ponomarev, Yu. N. Measurements of Air and Noble-Gas Broadening and Shift Coefficients of the Methane R_3 Triplet of the $2\nu_3$ Band. *Appl Phys B* **2001**, *72* (8), 953–959. https://doi.org/10.1007/s003400100586.

(27) Prokhorov, I.; Mohn, J. CleanEx – A Versatile Automated Methane Preconcentration Device for High-Precision Analysis of 13CH4, 12CH3D, and 13CH3D. **2022**. https://doi.org/10.6084/m9.figshare.20101910.


Air
$^{12}CH_4$
$^{13}CH_4$
$^{12}CH_3D$
$^{13}CH_3D$
N_2 O_2 Ar CO_2 CO